

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 08 June 2001 (08.06.01)	To: Commissioner US Department of Commerce United States Patent and Trademark Office, PCT 2011 South Clark Place Room CP2/5C24 Arlington, VA 22202 ETATS-UNIS D'AMERIQUE in its capacity as elected Office
International application No. PCT/US00/22616	Applicant's or agent's file reference TRANS 1 WO
International filing date (day/month/year) 18 August 2000 (18.08.00)	Priority date (day/month/year) 19 August 1999 (19.08.99)
Applicant VELANDER, William, Hugo	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

08 March 2001 (08.03.01)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Claudio Borton
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

REC'D 06 NOV 2001

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference TRANS 1 WO	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/22616	International filing date (day/month/year) 18/08/2000	Priority date (day/month/year) 19/08/1999	
International Patent Classification (IPC) or national classification and IPC A01K67/027			
Applicant US TRANSGENICS, INC. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 08/03/2001	Date of completion of this report 30.10.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Julia, P Telephone No. +49 89 2399 8410



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/22616

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-54 as originally filed

Claims, No.:

1-55 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5: This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/22616

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
 - copy of the earlier application whose priority has been claimed.
 - translation of the earlier application whose priority has been claimed.
2. This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

see separate sheet

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-27, 55
	No:	Claims 28-54
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-55
Industrial applicability (IA)	Yes:	Claims 1-27, 55
	No:	Claims 53-54 (see citations and explanations)

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/22616

claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/22616

1. Additional remarks to item II :

The priority documents pertaining to the present application were not available at the time of establishing this international preliminary examination report (IPER). Hence, the current assessment is based on the assumption that all claims enjoy priority rights from the filing date of the priority document (19.08.99).

2. Additional remarks to item V :

The present application discloses the production of a full-length human prothrombin in the milk of transgenic mice and pigs using the cis-acting expression signals of the mouse long whey acidic protein promoter (long WAP promoter) construct (examples 1-3).

As far as the present application does not disclose any specific technical feature which could differentiate the claimed prothrombin or prothrombin-related polypeptides (isolated from any transgenic organism!!) from (any!!!) prothrombin or prothrombin-related polypeptides from the known prior art (such as the ones referred in the description of the present application and/or documents cited in the ISR), the IPEA, in agreement with the comments made below under "Additional remarks to item VIII", considers that the subject matter of claims 28-54 does not fulfil the requirements of article 33 (2) and (3) PCT.

The following documents, cited in the International Search Report (ISR), have been found to be relevant for assessing the inventiveness of the claimed subject matter :

WO96/09377 (**D1**) discloses similar expression constructs (promoters) in similar transgenic organisms (mice, pig) than the ones of the present application. The teachings of this document are clearly said to be general even if they are concerned with the specific production of the human coagulation factor VIII and von Willebrand factor. Similar disclosures are found in documents WO94/05796 (**D2**) and W.H. Velander et al., Proc. Natl. Acad. Sci. USA 1992, Vol. 89, pages 12003-12007 (**D3**) which, however, are concerned with the specific production of human protein C. General methods for isolating recombinant (therapeutic) proteins from the milk of transgenic animals, including pig milk, are referred and exemplified in the documents A. Degener et al., J. Chromatography 1998, Vol. 799, pages 125-137 (**D4**) and T.D. Wilkins and W. Velander, J. Cell. Biol. 1992, Vol. 49, pages 333-338 (**D5**). Documents US5510248 (**D6**) and US5476777 (**D7**) are concerned with the production of recombinant (human) prothrombin and prothrombin-related polypeptides.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/22616

In view of this prior art, the IPEA considers that the substitution of well-known human blood coagulation cascade proteins for prothrombin in well-known expression systems (D1-D3 milk of transgenic pigs) would not have required any special inventive contribution from the person skilled in the art. It was obvious to do it and there was more than a reasonable expectation of success. Thus, the subject matter of claims 1-55 does not fulfil the requirements of article 33 (3) PCT.

The attention of the Applicant is also drawn to the fact that the subject matter of claims 53-54 is directed to methods for treatment of the human or animal body (insofar the claimed subject matter comprises embraces a method *in vivo* too) and thus, it may be excluded from examination by Article 34(4)(a)(i) PCT in combination with Rule 67(iv) PCT too. Furthermore, for such a subject matter no unified criteria exist in PCT for the assessment whether it is industrially applicable or not. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject matter of claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

3. Additional remarks to item VII :

the general wording "incorporated by reference" found in the description for several documents cited in as relevant prior art or background art can arise problems clarity and interpretation and several Offices, such as the EPO, do not allow it (see PCT International Preliminary Examination Guidelines, C-II, 4.4 et seq.).

4. Additional remarks to item VIII :

The following objections are also raised under **Article 6 PCT** concerning the clarity of the claims :

i) according to Article 6 PCT, the claims shall be clear and concise. The requirement that the claims shall be concise refers to the claims in their entirety as well as to individual claims. The number of claims must be reasonable in relation to the nature of the invention claimed, and undue repetition of wording, for example between one claim and another, should be avoided by the use of dependent form (see PCT Gazette, 29.10.98, PCT

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/22616

International Preliminary Examination Guidelines, Section IV, III-5.1). The present set of claims contains a large number of claims (55) which further repetition of wording among them.

ii) the subject matter of several claims (claim 1, 5, , 13, etc...) refers to general "non-human transgenic organisms" and thus, it includes such organisms as a "transgenic" fish, reptile, insect, etc... wherein for all these animals the present description is not enabling. Even if claims are actually limited to general "non-human transgenic mammals" (claims 2, 6, etc...) such a broad subject matter is not technically supported. Methods for producing mammalian transgenic animals are not general for all mammals and they depend on the specific mammal used. Several steps such as a suitable status (stage) of the egg for optimal introduction of the DNA construct(s), time of insertion of the egg into the oviduct or uterus, etc.. are critical for the success of the method. Furthermore, several mammalian species do not lend themselves applicable to the present technology used for transgenic mice (or sheep, rabbits, goats and cows), such as duckbill platypus, spiny anteaters (echidna, egg-laying mammals, etc.). The description is not enabling for whole range claimed, i.e. does not allow the skilled person to produce the claimed product (transgenic animal) in or for the whole range claimed (general animal kingdom). The specification only teaches the production of two single mammalian species, i.e. mice and pigs.

iii) article 6 PCT requires the claims to be clear, i.e. the subject matter of the claims "per se" must be clear from the wording of the claim alone (by explicit definition or otherwise) (see PCT International Preliminary Examination Guidelines, as in force from 09.10.98, III-4.2). The general wording "prothrombin-related polypeptide" without any further requirement or without further characterizing said polypeptide does not fulfill this condition (structurally related ? is 30% identity already related or not ??; functionally related ??, etc... is a polypeptide related to the biological function of prothrombin, such as several coagulation factors already related to prothrombin ??, etc...). In this respect, both the requirements of a particular specific activity (claims 11, 14, 18, etc...) and/or the presence of a general "region" having a percentage of structural identity are considered to be ambiguous and not able to overcome this clarity objection. As far as the standard reference used (homologous pure??), the activity conditions, etc... are not clearly indicated, the reference to the specific activity ("has is..."????) is considered to be unclear. Moreover, "a region" without further defining the length of said region is unclear too (claims 13, 16, 17, etc...). Thus, an arbitrary short region (2 or 3 residues !!!) will

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/22616

certainly have a 80 to 100 % identity to whatever desired protein including prothrombin.

iv) the attention of the Applicant is drawn to the fact that no unified criteria exist in PCT for the assessment of a "product-by-process" claim. The EPO, for example, considers that a process feature in a product claim can only be relied on for establishing novelty over the prior art, where use of that process necessarily means that the product has a particular characteristic and the skilled person following the teaching of the application would inevitably achieve that characteristic, would be aware of that characteristic, and would discard any product not having it. In the absence of this information, the IPEA considers that the subject matter of claims directed to general prothrombin or prothrombin-related polypeptides only characterized by being isolated from a transgenic organism is not different from other prothrombin or prothrombin-related polypeptides from the known prior art.

v) moreover, as far as the claims are directed to general transgenic organisms and the specific post-translational modification associated to these transgenic organism is not explicitly and clearly disclosed in the application, the IPEA considers that claims requiring the claimed prothrombin or prothrombin-related polypeptides to be different from "naturally occurring prothrombin polypeptides" are only worded in terms of the result desired to be achieved. These claims are not actually supported and in the absence of any specific information concerning the particular post-translational modification meant, the IPEA considers that the claimed subject matter is not actually different from the one available in the known prior art (such as for instance a human recombinant prothrombin produced in mouse cells, monkey cells, CHO, COS, etc...).

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/22616

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	A01K67/027	C07K14/745	C12N15/67	G01N33/50	A61K35/20
	A61K35/16	A61K38/36	A61P7/04		

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 96 09377 A (AMERICAN NAT RED CROSS ;VIRGINIA TECH INTELL PROP (US)) 28 March 1996 (1996-03-28)</p> <p>page 4, line 13 -page 5, line 16; examples 1-3 & US 5 880 327 A 9 March 1999 (1999-03-09) cited in the application</p> <p>---</p> <p>-/-</p>	<p>1-3,5-9, 11, 22-27, 40,50-55</p>

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

17 January 2001

Date of mailing of the international search report

24/01/2001

Name and mailing address of the ISA

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Authorized officer

Mateo Rosell, A.M.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/22616

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 94 05796 A (AMERICAN NAT RED CROSS ;US ARMY (US)) 17 March 1994 (1994-03-17) page 5, line 30 -page 9, line 32 examples 1-11 & US 5 831 141 A 3 November 1998 (1998-11-03) cited in the application ---	1-3,5-9, 11,12, 21-27, 32,39, 40,50-55
A	VELANDER W H ET AL: "HIGH-LEVEL EXPRESSION OF A HETEROLOGOUS PROTEIN IN THE MILK OF TRANSGENIC SWINE USING THE CDNA ENCODING HUMAN PROTEIN C" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,NATIONAL ACADEMY OF SCIENCE. WASHINGTON,US, vol. 89, December 1992 (1992-12), pages 12003-12007, XP000919001 ISSN: 0027-8424 cited in the application the whole document ---	1-10,12, 21-27, 29,30, 40-42, 49-55
A	DEGENER A ET AL: "Zn-selective purification of recombinant proteins from the milk of transgenic animals" JOURNAL OF CHROMATOGRAPHY A,NL,ELSEVIER SCIENCE, vol. 799, no. 1-2, 13 March 1998 (1998-03-13), pages 125-137, XP004111379 ISSN: 0021-9673 the whole document ---	28,40
A	WILKINS T D ET AL: "ISOLATION OF RECOMBINANT PROTEINS FROM MILK" JOURNAL OF CELLULAR BIOCHEMISTRY,US,LISS, NEW YORK, NY, vol. 49, no. 4, 1 August 1992 (1992-08-01), pages 333-338, XP000611844 ISSN: 0730-2312 the whole document ---	28,40
A	US 5 510 248 A (MACGILLIVRAY ROSS T A ET AL) 23 April 1996 (1996-04-23) column 2, line 61 -column 3, line 18; figure 1 column 3, line 55 -column 4, line 67 ---	29-31, 41-43
		-/-

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 00/22616

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 476 777 A (FOSTER DONALD C ET AL) 19 December 1995 (1995-12-19) column 2, line 20-42 column 3, line 30 -column 4, line 16 column 5, line 4-38; examples 3,5 ----	29-31, 41-43
A	EP 0 229 234 A (BOEHRINGER MANNHEIM GMBH) 22 July 1987 (1987-07-22) abstract; example 4 -----	12, 49

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/22616

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9609377	A 28-03-1996	US CA EP JP	5880327 A 2200610 A 0807170 A 10506013 T		09-03-1999 28-03-1996 19-11-1997 16-06-1998
WO 9405796	A 17-03-1994	US CA EP JP US	5831141 A 2144333 A 0662138 A 8501936 T 5965789 A		03-11-1998 17-03-1994 12-07-1995 05-03-1996 12-10-1999
US 5510248	A 23-04-1996		NONE		
US 5476777	A 19-12-1995	US US AT AU AU CA DE DE DK EP ES FI GR JP NO WO	5527692 A 5502034 A 179754 T 683834 B 3428793 A 2125783 A 69229126 D 69229126 T 624199 T 0624199 A 2134836 T 943122 A 3030820 T 7502659 T 942456 A 9313208 A		18-06-1996 26-03-1996 15-05-1999 27-11-1997 28-07-1993 08-07-1993 10-06-1999 30-12-1999 01-11-1999 17-11-1994 16-10-1999 29-06-1994 30-11-1999 23-03-1995 29-06-1994 08-07-1993
EP 0229234	A 22-07-1987	DE AU AU JP	3536903 A 569433 B 6412686 A 62093665 A		16-04-1987 28-01-1988 14-05-1987 30-04-1987

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference TRANS 1 WO	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 22616	International filing date (<i>day/month/year</i>) 18/08/2000	(Earliest) Priority Date (<i>day/month/year</i>) 19/08/1999
Applicant US TRANSGENICS, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of **5** sheets.
 It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

US 00/22616

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A01K67/027 C07K14/745 C12N15/67 G01N33/50 A61K35/20
A61K35/16 A61K38/36 A61P7/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 96 09377 A (AMERICAN NAT RED CROSS ; VIRGINIA TECH INTELL PROP (US)) 28 March 1996 (1996-03-28)</p> <p>page 4, line 13 -page 5, line 16; examples 1-3 & US 5 880 327 A 9 March 1999 (1999-03-09) cited in the application</p> <p>---</p> <p style="text-align: center;">-/--</p>	1-3, 5-9, 11, 22-27, 40, 50-55

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

17 January 2001

24/01/2001

Name and mailing address of the ISA

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Authorized officer

Mateo Rosell, A.M.

INTERNATIONAL SEARCH REPORT

International Application No

US 00/22616

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	DEGENER A ET AL: "Zn-selective purification of recombinant proteins from the milk of transgenic animals" JOURNAL OF CHROMATOGRAPHY A, NL, ELSEVIER SCIENCE, vol. 799, no. 1-2, 13 March 1998 (1998-03-13), pages 125-137, XP004111379 ISSN: 0021-9673 the whole document ----	28,40
A	WILKINS T D ET AL: "ISOLATION OF RECOMBINANT PROTEINS FROM MILK" JOURNAL OF CELLULAR BIOCHEMISTRY, US, LISS, NEW YORK, NY, vol. 49, no. 4, 1 August 1992 (1992-08-01), pages 333-338, XP000611844 ISSN: 0730-2312 the whole document ----	28,40
A	US 5 510 248 A (MACGILLIVRAY ROSS T A ET AL) 23 April 1996 (1996-04-23) column 2, line 61 -column 3, line 18; figure 1 column 3, line 55 -column 4, line 67 ----	29-31, 41-43
		-/-

INTERNATIONAL SEARCH REPORT

International Application No

US 00/22616

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 476 777 A (FOSTER DONALD C ET AL) 19 December 1995 (1995-12-19) column 2, line 20-42 column 3, line 30 -column 4, line 16 column 5, line 4-38; examples 3,5 -----	29-31, 41-43
A	EP 0 229 234 A (BOEHRINGER MANNHEIM GMBH) 22 July 1987 (1987-07-22) abstract; example 4 -----	12, 49

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

US 00/22616

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9609377	A 28-03-1996	US 5880327 A CA 2200610 A EP 0807170 A JP 10506013 T		09-03-1999 28-03-1996 19-11-1997 16-06-1998
WO 9405796	A 17-03-1994	US 5831141 A CA 2144333 A EP 0662138 A JP 8501936 T US 5965789 A		03-11-1998 17-03-1994 12-07-1995 05-03-1996 12-10-1999
US 5510248	A 23-04-1996	NONE		
US 5476777	A 19-12-1995	US 5527692 A US 5502034 A AT 179754 T AU 683834 B AU 3428793 A CA 2125783 A DE 69229126 D DE 69229126 T DK 624199 T EP 0624199 A ES 2134836 T FI 943122 A GR 3030820 T JP 7502659 T NO 942456 A WO 9313208 A		18-06-1996 26-03-1996 15-05-1999 27-11-1997 28-07-1993 08-07-1993 10-06-1999 30-12-1999 01-11-1999 17-11-1994 16-10-1999 29-06-1994 30-11-1999 23-03-1995 29-06-1994 08-07-1993
EP 0229234	A 22-07-1987	DE 3536903 A AU 569433 B AU 6412686 A JP 62093665 A		16-04-1987 28-01-1988 14-05-1987 30-04-1987

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/22616

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	A01K67/027	C07K14/745	C12N15/67	G01N33/50	A61K35/20
	A61K35/16	A61K38/36	A61P7/04		

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WO 96 09377 A (AMERICAN NAT RED CROSS ;VIRGINIA TECH INTELL PROP (US)) 28 March 1996 (1996-03-28)</p> <p>page 4, line 13 -page 5, line 16; examples 1-3 & US 5 880 327 A 9 March 1999 (1999-03-09) cited in the application</p> <p>---</p> <p style="text-align: center;">-/--</p>	1-3,5-9, 11, 22-27, 40,50-55



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search

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Int'l. Application No

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A	WO 94 05796 A (AMERICAN NAT RED CROSS ;US ARMY (US)) 17 March 1994 (1994-03-17) page 5, line 30 -page 9, line 32 examples 1-11 & US 5 831 141 A 3 November 1998 (1998-11-03) cited in the application	1-3,5-9, 11,12, 21-27, 32,39, 40,50-55
A	VELANDER W H ET AL: "HIGH-LEVEL EXPRESSION OF A HETEROLOGOUS PROTEIN IN THE MILK OF TRANSGENIC SWINE USING THE cDNA ENCODING HUMAN PROTEIN C" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, US, vol. 89, December 1992 (1992-12), pages 12003-12007, XP000919001 ISSN: 0027-8424 cited in the application the whole document	1-10,12, 21-27, 29,30, 40-42, 49-55
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A	US 5 510 248 A (MACGILLIVRAY ROSS T A ET AL) 23 April 1996 (1996-04-23) column 2, line 61 -column 3, line 18; figure 1 column 3, line 55 -column 4, line 67	29-31, 41-43
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International Application No
PCT/US 00/22616

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 476 777 A (FOSTER DONALD C ET AL) 19 December 1995 (1995-12-19) column 2, line 20-42 column 3, line 30 -column 4, line 16 column 5, line 4-38; examples 3,5 -----	29-31, 41-43
A	EP 0 229 234 A (BOEHRINGER MANNHEIM GMBH) 22 July 1987 (1987-07-22) abstract; example 4 -----	12,49

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US 5510248	A 23-04-1996	NONE			
US 5476777	A 19-12-1995	US 5527692 A US 5502034 A AT 179754 T AU 683834 B AU 3428793 A CA 2125783 A DE 69229126 D DE 69229126 T DK 624199 T EP 0624199 A ES 2134836 T FI 943122 A GR 3030820 T JP 7502659 T NO 942456 A WO 9313208 A			18-06-1996 26-03-1996 15-05-1999 27-11-1997 28-07-1993 08-07-1993 10-06-1999 30-12-1999 01-11-1999 17-11-1994 16-10-1999 29-06-1994 30-11-1999 23-03-1995 29-06-1994 08-07-1993
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